

Letters

RESEARCH LETTER

Life Expectancy in Patients With Chronic HCV Infection and Cirrhosis Compared With a General Population

Almost 3 million people in the United States are chronically infected with the hepatitis C virus (HCV).¹ The life expectancy of patients with chronic HCV infection is reduced compared with the general population, largely attributable to the development of cirrhosis, liver failure, and hepatocellular carcinoma.²

We³ and others have shown that the hazard of all-cause mortality is lower among patients with chronic HCV infection and advanced hepatic fibrosis if sustained virological response (SVR) is attained, but comparisons have been limited to those without SVR.³ To further investigate the advantage of attaining SVR, we compared overall survival of patients with chronic HCV infection and bridging fibrosis or cirrhosis before therapy (with and without SVR) with that of the general population.

Methods | We used data on patients with chronic HCV and advanced hepatic fibrosis from a previous study; the design and characteristics of the population have been described in detail.³ The ethics committees at the individual centers approved the study. Written or oral informed consent was obtained from all patients.

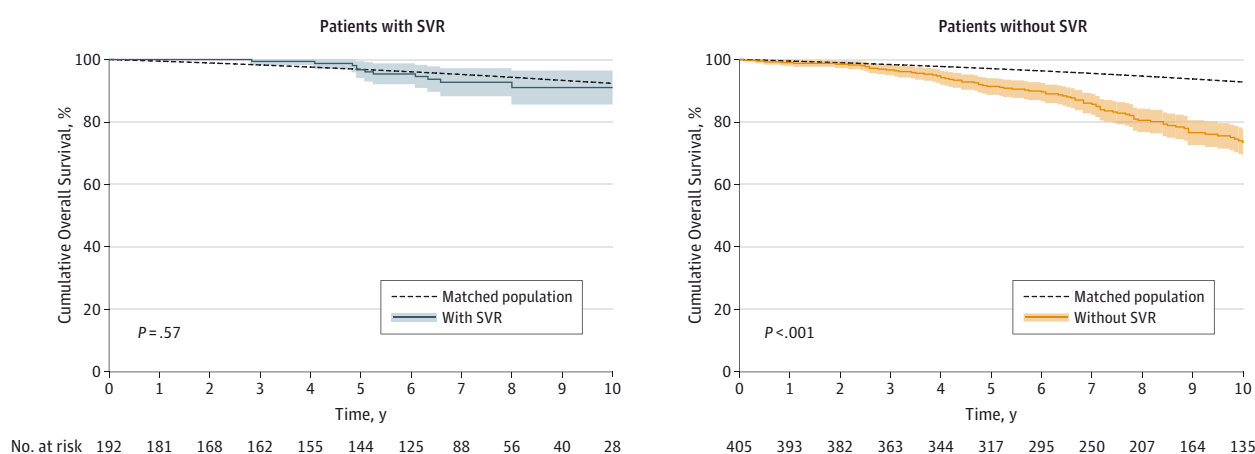
All consecutive patients with chronic HCV monoinfection and biopsy-proven advanced hepatic fibrosis (Ishak fi-

brosis scores 4, 5, or 6) who initiated interferon-based antiviral therapy between 1990 and 2003 from 5 large hepatology units in Europe and Canada were included. Follow-up started 24 weeks after cessation of antiviral treatment, at which time achievement of SVR (defined as HCV RNA negativity in a blood sample using molecular assays) was determined. If the survival status as of January 1, 2010, could not be determined from retrospective chart review, the patient, primary care physician, or both were recontacted. If this was not successful by October 2011, the follow-up was considered incomplete.

For each virological response group, the observed overall survival was compared with the expected survival from matched age-, sex- and calendar time-specific death rates of the general population in the Netherlands, which were obtained from the bureau of statistics, using the life table method and the Wilcoxon (Gehan) test. The statistical tests were 2-sided and $P < .05$ was considered statistically significant. SPSS version 21.0 (SPSS Inc) was used for the statistical analyses.

Results | In total, 530 patients were followed up for a median of 8.4 years (interquartile range [IQR], 6.4-11.4 years). Follow-up was complete in 454 patients (86%). The median age was 48 years (IQR, 42-56 years), 369 patients (70%) were male, and 192 attained SVR (36%). Thirteen patients with SVR died, resulting in a cumulative 10-year overall survival of 91.1% (95% CI, 85.5%-96.7%), which did not differ significantly from the age- and sex-matched general population ($P = .57$) (Figure).

Figure. Overall Survival in Patients With Chronic Hepatitis C Virus Infection and Advanced Hepatic Fibrosis With and Without Sustained Virological Response (SVR) Compared With an Age- and Sex-Matched General Population



Time zero is 24 weeks following cessation of antiviral therapy, at which time it was determined whether patients attained SVR. The survival curves among the patients with chronic hepatitis C virus infection were constructed using a clock-reset approach, by which patients were allowed to switch from the group without SVR to the group with SVR as a result of successful retreatment during follow-up. In these cases, patients in the group without SVR were censored at

the time of SVR, which was then redefined as time zero for their further follow-up in the group with SVR. For each virological response group, the survival was compared with matched age-, sex-, and calendar time-specific death rates of the general Dutch population. The P values were based on the Wilcoxon (Gehan) test. The gray areas represent the 95% confidence intervals of cumulative survival among patients with and patients without SVR.

In contrast, 100 patients without SVR died. The cumulative 10-year survival was 74.0% (95% CI, 71.6%-79.8%), which was significantly lower compared with the matched general population ($P < .001$).

Discussion | Among patients with chronic HCV infection and bridging fibrosis or cirrhosis, attaining SVR was associated with survival comparable with that of the general population, whereas not attaining SVR was associated with reduced survival. The excellent survival among patients with advanced liver disease and SVR might be explained by the associations between SVR and regression of hepatic inflammation and fibrosis, reduced hepatic venous pressure gradient, reduced occurrence of hepatocellular carcinoma and liver failure, as well as reduced occurrence of diabetes mellitus, end-stage renal disease, and cardiovascular events.^{4,5} Even though patients with cirrhosis and SVR remain at risk for hepatocellular carcinoma, the annual hepatocellular carcinoma incidence is low and survival is substantially better compared with those without SVR.⁶ Competing risks could also contribute.

Our study is limited by its retrospective design and restriction to general population data that only were available for the Netherlands. However, life expectancy in the Netherlands is similar to other participating countries so this is not expected to have had a major influence on our results. Also, all patients received interferon-based therapy. Thus, these results need to be confirmed when interferon-free therapy is widely used because these highly effective regimens may be administered to patients with more comorbidity and more advanced liver disease.

Adriaan J. van der Meer, MD, PhD

Heiner Wedemeyer, MD, PhD

Jordan J. Feld, MD

Jean-François Dufour, MD, PhD

Stefan Zeuzem, MD, PhD

Bettina E. Hansen, PhD

Harry L. A. Janssen, MD, PhD

Author Affiliations: Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands (van der Meer, Hansen, Janssen); Department of Gastroenterology, Hepatology, and Endocrinology, Medical School Hannover, Hannover, Germany (Wedemeyer); Toronto Centre for Liver Disease, University Health Network, Toronto, Ontario, Canada (Feld); Department of Clinical Research, University of Bern, Bern, Switzerland (Dufour); Medizinische Klinik I, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt, Germany (Zeuzem).

Corresponding Author: Adriaan J. van der Meer, MD, PhD, Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Gravendijkwal 230, 3015 CE Rotterdam, the Netherlands (a.vandermeer@erasmusmc.nl).

Author Contributions: Drs van der Meer and Janssen had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: All authors.

Acquisition, analysis, or interpretation of data: Van der Meer, Dufour, Zeuzem, Hansen, Janssen.

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COMMENT & RESPONSE

Erythropoietin for Traumatic Brain Injury

To the Editor Dr Robertson and colleagues¹ conducted a 2 × 2 factorial design randomized clinical trial of 200 patients with traumatic brain injury to test the effect of 2 approaches to trans-